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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/624,006	07/21/2003	Alfredo Emilio De Ioannes	IOA-001	5632

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EXAMINER	
MAYER, SUZANNE MARIE	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/624,006	IOANNES ET AL.	
	Examiner	Art Unit	
	Suzanne M. Mayer, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-20 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-20 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 21 July 2003 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Upon reconsideration, the examiner has determined that no undue burden exists and hereby withdraws the restriction requirement. Therefore all claims have been examined.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 2 provides for the use of the product according to claim 1 as an immunostimulant, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to claim as their invention. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 2 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

4. Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites a method according to Claim 6 wherein the

composition further comprises "an other" protein etc. The proper spelling and use of the word "another" in this instant will overcome this rejection.

5. Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites a method of "administrating". Amendment "administering" will overcome this rejection.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 14 and 16-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 14 and 16-18 are drawn to a method of administration of CCH-A with a hapten or peptide for claims 14 and 16, and an additional protein in claims 17 and 18. While the specification is enabling for the co-administration of a hapten, it is unclear whether any peptide or other protein will enhance the immunogenicity of any other peptide/protein by simply administering it along with CCH-A. Therefore, it does not enable one skilled in the art how to make or use the invention without undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In the instant case, the quantity of experimentation would be large since there is a myriad of peptides to choose from. The amount of guidance in the specification is zero with regard to what peptides or other proteins might have enhanced immunogenicity when complexed to CCH-A. No working examples are present for any peptides or other proteins. The nature of the invention is such that many different peptides and proteins of many different lengths and biological activities may or may not have enhanced immunogenicity by simply complexing with CCH-A and there may be no

way to test for this. The state of the prior art is that many different peptides and other proteins with different biological activities exist that might or might not display enhanced immunogenicity when complexed with CCH-A. The relative level of skill in this art is very high. The predictability as to what peptides or other proteins will have enhanced immunogenicity activity is zero.

When the factors are considered in their entirety, the Wands analysis dictates a finding of undue experimentation and thus, the claims are not enabled.

8. Claims 14 and 16-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 14 and 16-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of enhancing the immunogenicity of a hapten or peptide as recited in claims 14 and 16, or any other protein as recited in claims 17

and 18, when complexed to CCH-A. The claims do not require that the peptides or other proteins possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a method of use of an undefined genus of peptides or proteins; ultimately, these claims encompass every known and unknown peptide and protein that exists.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, there is not even identification of any particular type of peptide or protein which might actually complex with CCH-A, let alone which ones might have enhanced immunogenicity upon doing so. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description.

Vas-Cath Inc. V. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed."* The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." As discussed above, the skilled artisan cannot envision the detailed peptides or proteins, and therefor conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the methods of making the

claimed invention. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating or making it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

12. Claims 1 and 3-5 are rejected under 35 U.S.C. 102(b) as being anticipated by the 2000-2001 Calbiochem catalog and by Becker et al.

13. Hemocyanin from *Concholepas concholepas* is disclosed on p. 730 of the Calbiochem general catalog. The catalog states that the composition is available in a sterile form, in a physiologically acceptable buffer that lacks magnesium or calcium and contains the entire CCH protein (e.g. CCH-A and CCH-B). Becker et al. teach the various molecular weights of the individual CCH-A and CCH-B subunits and that CCH has been successfully used an immunogen carrier protein. The claim language of the instant claims uses open language which allows for a broader interpretation of these claims, e.g. in claim 1 'comprising of' allows for a composition which contains CCH-A amongst other things. Therefore, to meet the limitation of claim 1, the examiner need only find a composition which contains CCH-A in it. The subsequent rejected claims have been interpreted in an analogous manner in that the product disclosed in the Calbiochem catalog comprises both CCH-A and CCH-B.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

16. Claims 6-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Linn et al. in view of Becker et al. and the 2000-2001 Calbiochem catalog.

Linn et al. teach the use of KLH as a successful immunogen carrier in the treatment of experimental bladder cancer. Specifically, in one particular group of rats suffering from bladder cancer, systemic administration of KLH in a concentration of 5mg/ml was administered (p. 37, Materials and Methods, line 10) with results that indicated a significant decrease in tumor occurrence for this particular test group. Linn et al. also describe an experiment carried out by others (Lamm et al.) in which KLH is co-administered with Immunocothel, which is KLH modified for clinical use (p. 36, last paragraph), in the treatment in mice with bladder cancer. Therefore, Linn et al. teach an analogous use of KLH as compared to the use of CCH as set-forth in the rejected

claims. Linn et al., do not, however teach the use of CCH in the treatment of bladder cancer.

However, the fact that Linn et al. teach CCH, does not preclude that it would have been obvious to make the substitution of CCH for KLH when viewed in light of the opening recitation of the abstract whereby the following is divulged:

> Keyhole Limpet haemocyanin (KLH) is a high-molecular-weight protein antigen collected from the haemolymph of the sea mollusk *Megathura crenulata*. It is a powerful non-specific immune response modifier that induces both a cell-mediated and humoral response in animals and man. Thus, it is commonly used clinically as a measure of immune competence. In 1974, Olson studied the immune competence of bladder cancer patients by intradermal application of KLH. He later observed a significant reduction of recurrent disease in this patient group compared to another not immunized with KLH.

And when further consideration is given to the specification of the present application which recites on page 6, line 23:

> The over exploitation of the Keyhole limpet has resulted in a scarcity of KLH in the international market. The promissory results of immunostimulation and bladder caner immunotherapy have led to search for other molecules with similar properties. It is important to find alternative substances to replace or supplement KLH, where such new substances must present the adequate characteristics in relation to the immune response. In this context, hemocyanin from *Concholepas concholepas* is a good option to supplement the use of KLH.

The motivation why one skilled in the art would want to substitute CCH for KLH is further elucidated by Becker et al. who teach that hemocyanins, such as the Keyhole Limpet hemocyanin (KLH), are indeed potent immunostimulant agents which have been widely used in immunology and medicine and that *Concholepas concholepas* hemocyanin (CCH) belongs to this class of hemocyanins. Furthermore, CCH and has

successfully been used as immunogen carriers in the past (see meeting Abstract). An additional motivating factor for using CCH in exchange for KLH is taken in view of the Calbiochem catalog (p. 730, 2000-2001 catalog) for which the intended use of CCH is explained as follows:

> Convenient form which may be used directly for hapten conjugation. Displays similar features as KLHby electron microscopy, but with enhanced solubility. Highly immunogenic in invertebrates due to its phylogenetic distance from the vertebrates and high molecular weight.

Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to use CCH in place of KLH in methods where an immunogen carrier is needed because of the reasons illustrated above and to have the expection of success in doing so.

Conclusion

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suzanne M. Mayer, Ph.D. whose telephone number is 571-272-2924. The examiner can normally be reached Monday to Friday from 8.30am to 5.00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SMM
3 August, 2004

ROBERT A. WAX
PRIMARY EXAMINER